

THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH

66TH STREET AND YORK AVENUE
NEW YORK 21, N. Y.

October 2, 1952

Dear Josh:

I have been teaching myself to touch type and tried this that way. Too many errors and so I shall revert to the old system with probably as many errors.

Received your letter this noon while about to write you for some cultures. I feel rather chagrined but shall ask for them anyway. As long as the parent cultures are still viable any markers other than such as LA-22 should be recoverable. The strains lost represent my early attempts at lyophilization and I think that you will find the later ones, including the stock of Salmonella serotypes, in better condition.

I did not take many of the mutants with me and those were all on slants. I did take all of the original cultures that had been shipped to us by Lillengen, Edwards etc. and these seem to be in good condition.

I don't have a culture of SW-36, nor is there one available here. There are several mutant derivatives of this line in the collection; SW-77 through SW-83, SW-155 and SW-157. As I remember I chose those two cultures for the vaccine at random and used two on the theory that two is better than one. However I now feel that the use of any of the parental typhimuriums would suffice. I had recently occasion to titrate some of them in mice and all except SW-435 are virulent; including LT-2, 7, 22 and some of their mutants.

Stocker did a most beautiful job this summer. I spoke to him once and we were to get together again before he left to discuss writing this up. Due to a mix up in signals I was off to Ithaca and he sailed.

I agree about the spontaneous i from SW-543. Its origin is now quite clear to me. I always used heat inactivated FA ~~xx~~ in my controls. Its inactivation was measured on LA-22. It is probable that the preparation was not completely inactivated with regard to transmutilizing ability. The appearance of the i without b is interesting in that the frequency of the latter is so much greater. This may point to a differential viability and should be looked into further. I have obtained five more spontaneous b with no i. FA has been prepared from S. typhi and I'm looking for linked transduction here.

Yes it is too bad that there is no other case of linked transduction but when working between strains the characters involved must be linked in both receptor and donor and this may not occur for other than pseudoalleles. Even within a strain, where the kinds of characters that can be studied are fewer, the piece may only encompass a small segment with the only possibility for linked transduction between pseudoalleles. This seems to be the experience with pneumococcus and more recently with Hemophilus. I recently read Alexander's latest manuscript. There was a story very similar to the motility-antigen linked transduction. It is a fine piece of work but oh how it is written. She carries the DNA hypothesis to absurdity and has no comprehension of the genetics involved. By the way since Hershey's work DNA is it and one doesn't dare look even slightly critical.

Unfortunately all of the b serum was used up. The unknown serum is an S. pullorum serum which had been absorbed by typhimurium to remove the Xll.

I beg to differ with you in regard to the utility of gal-duction in unearthing the mechanism of transduction. There is an essential difference, two in fact, you state them quite explicitly, range and stability, both of which are probably tied up. Gal-duction, I believe, is more a very specialized case of transduction just as the lambda K-12 relationship is a specialized case of

lysogenicity. I don't comprehend what you mean about the clear cut types of response to lambda other than in the sense that I shall later mention the responses to the Salmonella phages which are as sharp as could be desired. From what Stocker said about the appearance of lambda amongst the transducibles I gather that you are implying that the phage may play other than a passive carrier role. This may be true in gal-duction but I don't believe it to be so in transduction wherein the immunes can be transduced while the phage disappears. This could be due to an irreversible binding of the phage and so I am setting up a more explicit test to prove the essential triviality of the phage other than as a carrier. By the use of plaque morphology mutants which are mutually exclusive I intend to show that the phage can be thrown out while the transduction occurs. Have you used any lysates other than those induced by U.V.? It is possible that the prior reduction of phage to pro-phage and its stabilization on the "chromosome" fixes the genetic material which may be picked up to that to which it has been linked. Lieb tells me that high titer lambda can be obtained directly by methods not different from those used to obtain high titer PLT-22; adjustment of the multiplicity with critical timing.

I am attempting to clear up the story on those cultures from which one can obtain self lytic phages. Here your remarks about extraneous phages is well taken as so far I've found three, at least two of which are different in kind; one may be a mutant of the other.

The lab is just about set up but I'm some discouraged. This commuting takes the spunk out of one. If the traffic goes well it only takes me thirty-five minutes, but there are times like this A.M. when I spent an hour and a half coming in. Also it is difficult not being able to get back in the evenings which necessitates all kinds of tricks to keep plaques from overgrowing by morning. The Institute is stiff and formal but other than wearing a tie, a suit coat and shaving regularly I don't notice it.

Besides giving what little help I can to Schneider on what seems to me an almost impossible problem (how does one ever control all of the variables in such a Gestalt?) I am, as you can surmise still playing with transduction. For the time being I shall attack the problem as a phage problem side by side with a transduction one. Transduction can occur when a strain is susceptible, immune-lysogenic and immune. It can also occur with a variety of phages grown on a variety of strains including the homologous and can be assayed quantitatively with numerous markers. ~~By the proper combination of these variables~~ With the optimism of a biologist I hope that by the proper combination of these variables ~~ix~~ I shall find a system with an efficiency so high that single particle analysis is feasible. This being so far away and with lord knows what sidetracks in between I think no further. I've already cut the phage to FA ratio a factor of 100 in the heterologous-donor, sensitive-indicator system with PLT-22. I hope for a factor of ten to hundred more when using the homologous donor. This sensitive indicator system is interesting per se as the dose response curve is quite linear even with multiplicity of infection well below one. How does the transduced cell survive infection if the same particle that can produce a plaque on it can also transduce it?

One problem I have solved and that is obtaining high titer phage for chemical analysis. About 10,000 phage particles are seeded into the soft agar layer. In time there is first a bacterial background and then a clearing (4-5 hours) at which time the layer is scrapped up and the phage eluted. Centrifugation and precipitation etc can be then used for further concentration and purification. This procedure works especially well with some "less temperate" variants I have, but also can be used for the temperate ones.

* Shades of P.F. Clark who was to see us recently and at lunch asked in front of all whether I'd rewritten that and manuscript.

Since the antigen story is in your's and Stocker's most capable hands, and the breeding program will be instituted at Chamblee I feel it is those directions mentioned above that I should continue my researches. I always did say I'd become a phagologist. The cultures desired are SW-534, 541, 569, SW-175 through 180, SW-258 through 260, SW-237 through 239, 240, 241 243, 245 246 and 248.

Our apartment is taking shape with the arrival of furniture and I did get a car. It, a 48 Plymouth, required some overhauling but now seems to be adequate for getting me to and from work.

Tell Esther that we'd be glad to join The C.U. group again and enclosed you will find a check. However since we have arrived here we have not received the reports although we guaranteed forwarding postage for our second class mail. Upon inquiry they claim to have no record of our membership and asked for such information as group members, leaders and if possible the cancelled voucher. ^{+date.} We gave them as much information as we could and have not heard from them for some time. Perhaps you might try to straighten them out.

My best to everybody.

Sincerely,



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